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Diffusion-Weighted Imaging of Traumatic Optic Neuropathy: Diagnosis and Predicting the Prognosis

Uttam Bodanapally, MD
Maj Andrew Choi, MD, USAF, MC
Robert Shin, MD

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Air Force Research Laboratory
711th Human Performance Wing
School of Aerospace Medicine
Air Force Expeditionary Medical Skills Inst
C-STARS Baltimore
2510 Fifth St.
Wright-Patterson AFB, OH 45433-7913

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Col Raymond Fang, USAF, MC, FS Chief, C-STARS Baltimore	Col Benjamin A. Harris, USAF, MC, SFS Chair, AF Expeditionary Medical Skills Inst

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Uttam Bodanapally, MD
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Robert Shin, MD

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14. ABSTRACT

Traumatic optic neuropathy is an axonal injury of the optic nerve fibers and occurs from a number of mechanisms both in blunt and penetrating trauma. Out of all the types of ocular injuries, traumatic optic neuropathy has one of the worst visual outcomes. For this study, we intended to use high-resolution diffusion-weighted magnetic resonance imaging (DW-MRI) to obtain sufficiently high resolution and detailed imaging of the optic nerve at two time points. This powerful tool has the potential to help predict the outcomes including the degree of vision recovery. We screened patients admitted to the University of Maryland Shock Trauma Center and attempted to recruit them for an initial DW-MRI during their hospital stay, with the intention of doing a 6-month follow-up. Due to uncontrollable circumstances, only one patient underwent MRI of the optic nerves according to the specified protocol. No significant findings or results were obtained from this study. If a follow-up appointment were not required for this study, more patients would have been receptive.

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Optic nerve injury, diffusion-weighted imaging, magnetic resonance imaging, traumatic optic neuropathy

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1.0 SUMMARY

The overall aim of this study was to explore the use of high-resolution diffusion-weighted magnetic resonance imaging (MRI) to diagnose and predict prognoses of traumatic optic neuropathy in a controlled prospective study. Patients admitted to the University of Maryland Shock Trauma Center with clinical diagnosis of optic nerve injury were imaged at or near time of admission and again at 3 and 6 months post injury. Clinical and radiological information was assessed to determine injury, expected outcome, and outcome after 6 months. The intention of this study was to develop an analytical multivariate model in which patient and injury information could predict outcome at 6 months with single admission imaging characteristics (diffusion tensor imaging measurement of the optic nerve).

Due to unexpected difficulties with enrollment, the study was only able to enroll two patients. These unforeseen difficulties included the critical condition of this patient population due to their associated traumatic brain injury. Transportation of the critically injured patient to an MRI scanner and performing a lengthy scanning procedure (approximately 40 minutes) for the sole purpose of research could not be justified. In addition, a significant number of patients with traumatic optic neuropathy had associated facial and orbital fractures. Management protocols at the Shock Trauma Center usually involve early facial fracture fixation with metallic plates (often in the initial 1 or 2 days). Performing MRI and obtaining diffusion tensor imaging sequences were not possible after fracture fixation due to the significant metallic artifacts around the optic nerves due to the close proximity of the hardware. Because of enrollment challenges, the study was terminated before enrollment goals were met.

2.0 INTRODUCTION

This report details the efforts of active recruitment, which began approximately 1 September 2012, for the Traumatic Optic Neuropathy (TON) Study.

3.0 BACKGROUND

3.1 Traumatic Optic Neuropathy

Traumatic optic neuropathy occurs from a number of mechanisms during combat injuries (blunt or penetrating): vasoconstriction of the optic nerve blood supply, shearing at the lamina cribrosa causing mechanical disruption, or a retrobulbar hemorrhage compressing the optic nerve. Optic neuropathy can also occur from hypotension. The data reported by Weichel et al. [1] of 523 consecutive globe or adnexal combat injuries, or both, sustained by 387 U.S. soldiers treated at Walter Reed Army Medical Center from 2003 to 2006 showed that of the ocular injuries treated, TON had one of the worst visual outcomes. TON remains a devastating problem that is a diagnostic and therapeutic challenge for both ophthalmologists and radiologists in spite of tremendous advances in magnetic resonance imaging (MRI) technology. There are no established imaging findings to diagnose this entity. Many patients who are clinically diagnosed with TON, however, appear to have normal imaging of the optic nerve on computed tomography and conventional MRI (so-called indirect TON) [2]. In fact, this limitation of conventional MRI warrants a strong need in this clinical context for further evaluation of the use of novel MRI techniques such as diffusion tensor imaging (DTI). With the potential of an increased number of

eye injuries (including TON) in the battlefield, a strong need exists to develop and evaluate MRI techniques such as DTI for early diagnosis and treatment of TON.

3.2 Diffusion Tensor Imaging

The ability to study the change in random motion of protons in water in vivo is the basis for diffusion-weighted imaging and DTI. DTI measures the signal change across multiple spatial directions and identifies the preferential directions of water diffusion, thus obtaining accurate measurements of water diffusion both longitudinally and transversely to optic nerve tracts. Such measurements are helpful in predicting axonal integrity, myelin disruption, and axonal swelling. Studies from our institution and others have established that reliable DTI data can be obtained from patients with acute spinal cord injury and that DTI measurements are more sensitive than conventional MRI in demonstrating the extent of spinal cord injury.

3.3 Preliminary Studies

No prior prospective studies have investigated the ability of DTI of the optic nerves to predict outcome in patients with TON. This powerful tool has the potential to provide valuable information beyond the spatial and anatomical resolution of conventional MRI regarding the integrity of optic tracts in TON and may help to predict outcomes including the degree of vision recovery.

4.0 METHODS

4.1 Patient Selection

Sixty participants (35 TON patients and 25 controls) were expected to be enrolled in 12 months from the University of Maryland Shock Trauma Center (STC) aged 17 or older. TON patients must have had a blunt or penetrating trauma and a clinical diagnosis of TON by an ophthalmologist. No participants could have any contraindications for MRI. Enrolled participants would be compensated $150 for completion of the follow-up visit. The study consented five participants (one expired, one withdrawn, 2 never imaged), with one captured TON volunteer. No follow-up visit was completed.

4.2 Procedures

Patients admitted to the STC with indications of head or face injury and potential optic nerve injury were imaged as part of standard of care with computed tomography at or near time of admission. The research staff members were notified of a potential patient once an ophthalmologist clinically diagnosed TON. The research staff determined eligibility on all participants using a standard of care MRI eligibility questionnaire prior to any diagnostic scans. Any medical conditions discovered that prohibited MRI scanning excluded participants from the study. All TON participants also underwent a 3- to 5-minute interview to collect information such as address and telephone numbers. This information allowed scheduled follow-up visits. The research staff scheduled the follow-up visits for the 3- to 6-month time point at an appropriate time.

Once study participants gave written consent for both the initial and follow-up visit diffusion-weighted magnetic resonance imaging (DW-MRI), the clinical staff organized and fulfilled the initial MRI before the patient was discharged from the STC. All participants had DW-MRIs performed, exclusively imaging the head/brain area. Each scan during MRI was as short as a minute or as long as 10 minutes. High-resolution DW-MRI imaging [multi-shot echo planar imaging (RESOLVE) and spin-echo based techniques (BLADE-DWI)] obtained sufficiently high resolution and detailed imaging of the optic nerves.

5.0 RESULTS

Limited patient population produced inadequate study enrollment. This study was unable to find any significant results.

Only one traumatic optic neuropathy patient was imaged. Representative images are shown below in Figure 1.

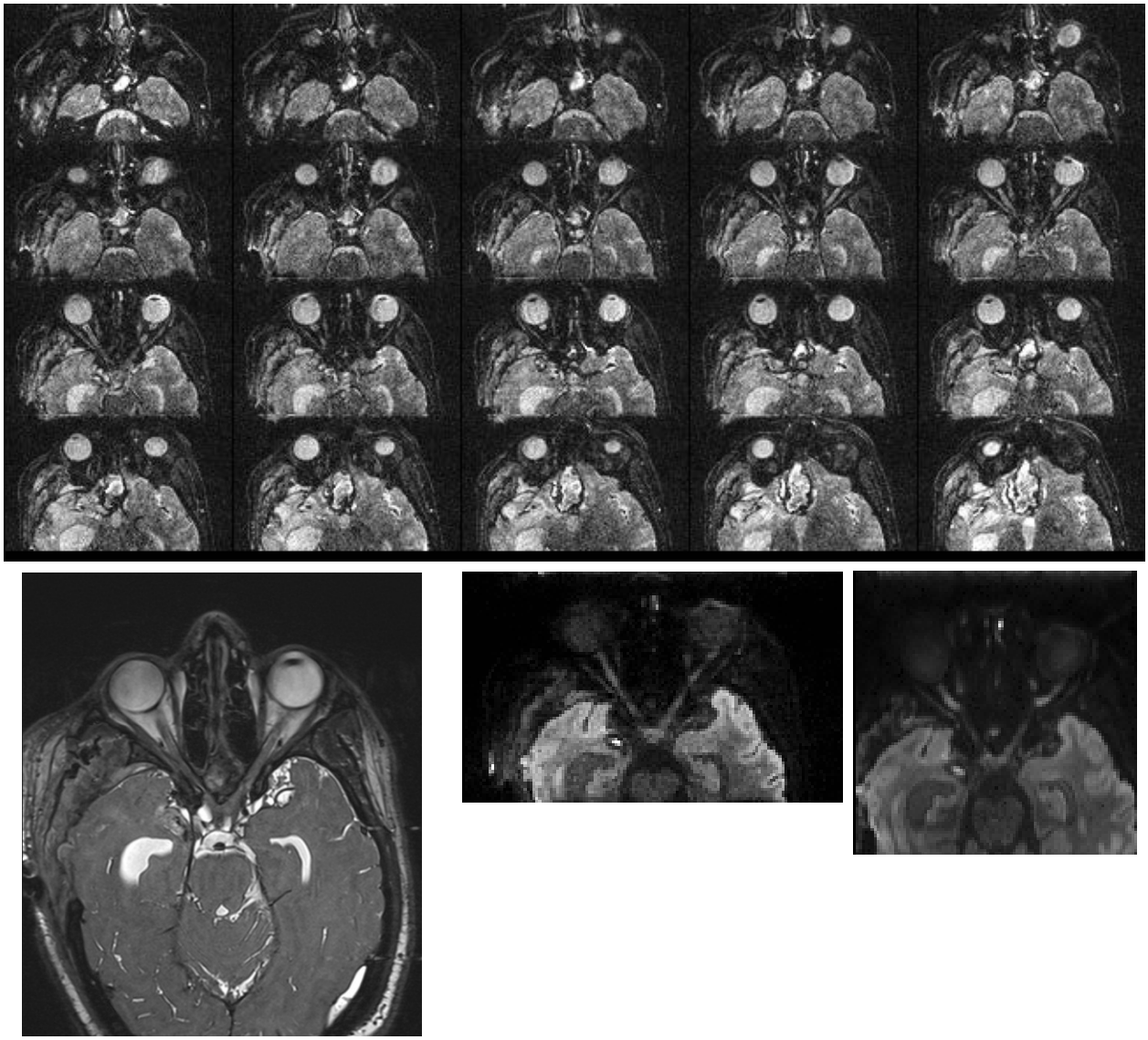

Figure 1. High-Resolution T2 Images from the First TON Patient Enrolled

6.0 DISCUSSION

This study was unable to demonstrate how DW-MRI could diagnose and predict recovery from TON because of low enrollment. Medical and social factors led to an inadequate study sample. Patients coming in with extensive trauma to the head and face are at risk of sustaining TON; however, the major concern for the patients' medical team is treating their primary injuries, which could include traumatic brain injury, facial fractures, or major orthopedic fractures. These treatment protocols include fixation with metallic plates or monitoring with metallic devices, which will eliminate them from obtaining MRIs. The majority of patients with TON would have severe traumatic brain injury, and because of the participants' likely altered mental status, obtaining consent from patients or their legally authorized representatives would be an obstacle.

The specialized patient population of diagnosed TON creates a very small sample size and difficulty for enrollment. A way to expand that population size could be to include patients who do not have a clinical diagnosis of TON. Perhaps if the standard of care criteria of needing an ophthalmology consult is met, such as signs of major facial trauma involving swollen shut eyes, orbital bone fractures, and muscle entrapment, then justification of enrollment could see if diagnoses can be made. Follow-up visits could be a reason why patients would not want to commit to the research; having one initial MRI before discharge could make a viable study. Also, without a follow-up MRI required, patients whose facial fractures were repaired via fixation could be enrolled in the study.

7.0 CONCLUSIONS

No significant conclusions were reached.

8.0 REFERENCES

1. Weichel ED, Colyer MH, Ludlow SE, Bower KS, Eiseman AS. Combat ocular trauma visual outcomes during Operations Iraqi and Enduring Freedom. Ophthalmology 2008; 115(12):2235-45.
2. Cockerham KP. Traumatic optic neuropathy. In: Ophthalmic care of the combat casualty. Falls Church, VA: Office of The Surgeon General, Department of the Army; 2003:395-403.

9.0 BIBLIOGRAPHY

Abbotts R, Harrison SE, Cooper GL. Primary blast injuries to the eye: a review of the evidence. J R Army Med Corps 2007; 153(2):119-23.

Belmont PJ Jr., Goodman GP, Zacchilli M, Posner M, Evans C, Owens BD. Incidence and epidemiology of combat injuries sustained during "the surge" portion of Operation Iraqi Freedom by a U.S. Army brigade combat team. J Trauma 2010; 68(1):204-10.

Blanch RJ, Scott RA. Military ocular injury: presentation, assessment and management. J R Army Med Corps 2009; 155(4):279-84.

Loy DN, Kim JH, Xie M, Schmidt RE, Trinkaus K, Song SK. Diffusion tensor imaging predicts hyperacute spinal cord injury severity. J Neurotrauma 2007; 24(6):979-90.

Mader TH, Carroll RD, Slade CS, George RK, Ritchey JP, Neville SP. Ocular war injuries of the Iraqi Insurgency, January-September 2004. Ophthalmology 2006; 113(1):97-104.
Mehta S, Agarwal V, Jiandani P. Ocular injuries in survivors of improvised explosive devices (IED) in commuter trains. BMC Emerg Med 2007; 7:16.
Pierpaoli C, Basser PJ. Toward a quantitative assessment of diffusion anisotropy. Magn Reson Med 1996; 36(6):893-906.
Steinsapir KD, Goldberg RA. Traumatic optic neuropathy. In: Miller NR, Newman NJ, Biousse V, Kerrison JB, eds. Walsh and Hoyt's clinical neuro-ophthalmology, 6th ed., vol. 1. Philadelphia: Lippincott Williams & Wilkins; 2005:438.
Thach AB, Johnson AJ, Carroll RB, Huchun A, Ainbinder DJ, Stutzman RD, et al. Severe eye injuries in the war in Iraq, 2003-2005. Ophthalmology 2008; 115(2):377-82.
Wade AL, Dye JL, Mohrle CR, Galarneau MR. Head, face, and neck injuries during Operation Iraqi Freedom II: results from the US Navy-Marine Corps Combat Trauma Registry. J Trauma 2007; 63(4):836-40.

LIST OF ABBREVIATIONS AND ACRONYMS

DTI	diffusion tensor imaging
DW-MRI	diffusion-weighted magnetic resonance imaging
MRI	magnetic resonance imaging
STC	Shock Trauma Center
TON	traumatic optic neuropathy